Nanomaterials Based on Poly(epsilon-caprolactone) - The Versatile and Intriguing Biomedical Building Block

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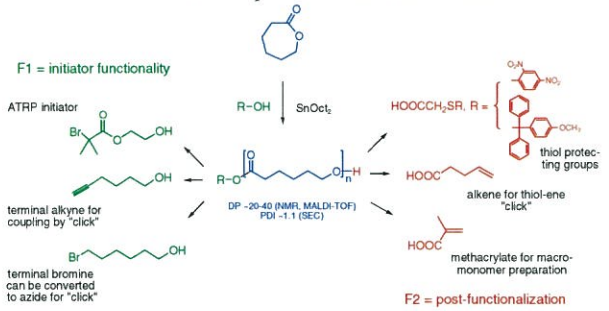
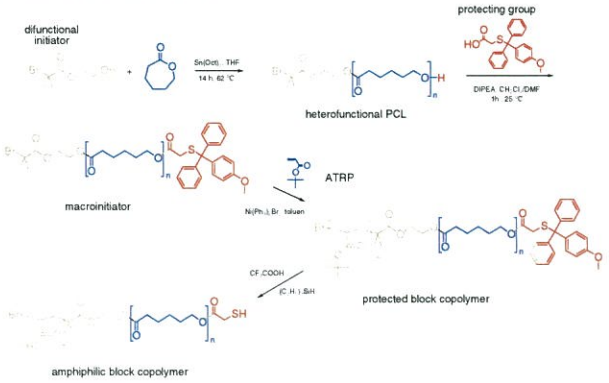
The classical medical material workhorse, poly(ε-caprolactone) (PCL), has been employed as a viable scaffold for design of several novel nanomaterials with intriguing, potentially therapeutic and biological properties. Living ROP strategies have afforded telechelic PCLs that can be utilized in either ATRP to make amphiphilic block copolymers or various "click" reactions resulting in multicomponent nanomaterials as outlined in Scheme 1. Three different examples will be elaborated.



Scheme 1. Various options for creating hetero bifunctional PCL building blocks by use of functional initiators (F1) and post-functionalization (F2).

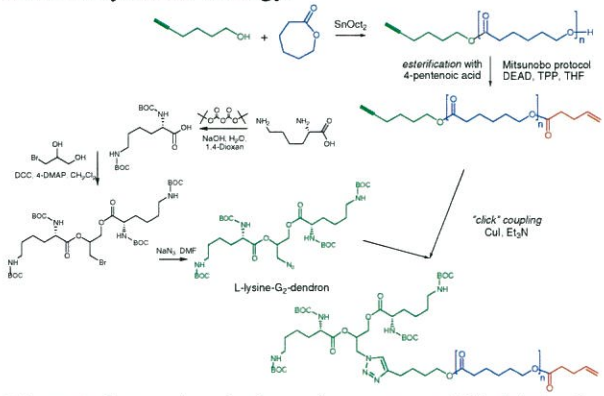
In the first case gold nanoparticles protected with a polymeric shell may combine ablative therapy and site-specific drug delivery in bladder cancer therapy [1]. This may be accomplished by tailoring the surface properties and the size of the gold clusters. The former may be addressed by devising polymeric ligands with desirable features and functional groups. Thus the preparation of the PCL-*b*-PAA corona will be outlined as shown in Scheme 2.



Scheme 2. Synthetic sequence for preparation of amphiphilic block copolymer precursor.

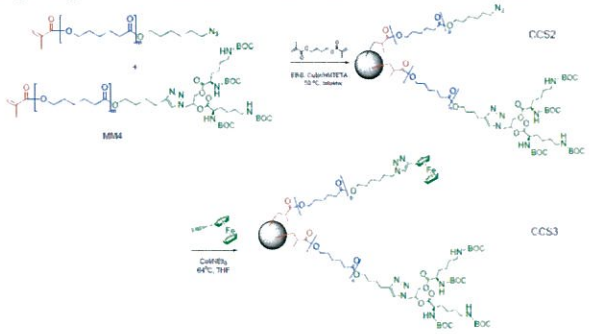
The synthesis of the effective macro-ligand that allows preparation of the stable gold cluster and provides nanoenvironment for hydrophobic anticancer drugs and mucoadhesive anchoring on mucous membranes is one of the objectives of this study.

The second approach is the ligation of biologically active moieties to the termini of a hydrophobic polymeric chain (PCL) to afford the amphiphilic linear-dendritic macromolecule that comprises rod-like, coil-like, and dendritic fragments [2]. Furthermore this may self-assemble in solid state as well as in aqueous solution. The facile route to linear-dendritic cholesteryl-*b*-PCL-*b*-(L-lysine)$_{G2}$ by thiol-ene and azide-alkyne "click" reactions is illustrated in Scheme 3. Here the driving motivation was to contrive a robust, facile, and effective synthetic strategy.



Scheme 3. Preparation of α-hexynyl-ω-pentenoate PCL, L-lysine-G_2-dendron, and the CuAAC coupling to the L-lysine-G_2-dendron-PCL.

Finally, the preparation of PCL-based miktoarm core-crosslinked amphiphilic star copolymers (CCS) with hydrophobic interior, charged hydrophilic surface, and targeting motifs are elaborated as shown in Scheme 4.



Scheme 4. Preparation of miktoarm CCS copolymers by copolymerization of functional macroinitiators.

Such nanoscopic core-shell type architectures are envisioned to be excellent candidates as drug delivery devices owing to the enhanced stability in biological fluids [3]. Moreover, they may permit site-specific delivery of their potential cargo due to the presence of biologically active moieties on the peripheries.

References:

1) I. Javakhishvili, S. Hvilsted, *Biomacromolecules* **10** (2009) 74-81.
2) I. Javakhishvili, W. H. Binder, S. Tanner, and S. Hvilsted, *Polymer Chemistry* **1** (2010) 506-513.
3) I. Javakhishvili and S. Hvilsted, *Polymer Chemistry* **1** (2010) 1650-1661.

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